



# UNITED STATES PATENT AND TRADEMARK OFFICE

72

UNITED STATES DEPARTMENT OF COMMERCE  
United States Patent and Trademark Office  
Address: COMMISSIONER FOR PATENTS  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/890,053	10/19/2001	Apollon Papadimitriou	CIBT-P01-097	4732
28120	7590	01/29/2004	EXAMINER	
ROPES & GRAY LLP ONE INTERNATIONAL PLACE BOSTON, MA 02110-2624			O HARA, EILEEN B	
			ART UNIT	PAPER NUMBER
			1646	

DATE MAILED: 01/29/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/890,053

Applicant(s)

PAPADIMITRIOU ET AL.

Examiner

Eileen O'Hara

Art Unit

1646

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 30 October 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-10 is/are pending in the application.
- 4a) Of the above claim(s) 9 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-8 and 10 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. §§ 119 and 120**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☒ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.  
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_ 6) ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

1. Claims 1-10 are pending in the instant application. Claims 1 and 4-8 have been amended as requested by Applicant in the Paper filed October 30, 2003.

#### ***Election/Restrictions***

2. Applicant's confirmation of election of Group I in the Paper filed Oct. 30, 2003 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claim 9 is withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the Paper filed Oct. 30, 2003.

Claims 1-8 and 10 are currently under examination.

#### ***Withdrawn Objections and Rejections***

3. Any objection or rejection of record which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

#### ***Double Patenting***

4. Claims 1-8 and 10 remain rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-19 of U.S. Patent No. 6,207,718, for reasons of record in the previous Office Action, at pages 5-6.

Art Unit: 1646

Applicant's contend that the present application and the cited patent are currently owned by the same party, and that Applicant's submission of a terminal disclaimer and a declaration under 37 CFR 1.130 will obviate these rejections. Applicant's request that the grounds of rejection be held in abeyance until the indication of otherwise allowable subject matter have been considered but not deemed persuasive, and the rejection is maintained.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 1-8 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pepinsky et al., U.S. Patent No. 6,444,793, filed 12/3/97, (provisionals filed 9/10/98, 6/17/98, 3/20/98 and 12/3/97) in view of Easton et al., U.S. Patent No. 4,614,794, issued Sept. 30, 1986,

and further in view of Usala et al., U.S. Patent No. 6,231,881, filing date July 10, 1998, for reasons of record in the previous Office Action, at pages 7-11, and below.

Claims 7 and 10 were mistakenly omitted from the previous rejection.

Claims 1-8 and 10 encompass pharmaceutical compositions containing hydrophobically modified hedgehog protein and a biodegradable protein as carrier, wherein the carrier may be soluble or insoluble cross-linked collagen, wherein the composition may also contain hyaluronic acid or alginate and further may contain arginine, and wherein the hedgehog protein is at a concentration of 0.1-100 mg/ml, wherein the composition is buffered in a range between 4.5 and 10, process for the production of a pharmaceutical composition wherein a hydrophobically modified hedgehog protein is combined in a therapeutically effective amount with arginine and a biodegradable protein as carrier.

The teachings of Pepinsky et al., Easton et al., and Usala et al. were discussed in the previous Office Action. Applicants traverse the rejection and assert that the rejection is moot in the light of the amended claims (1 and 8), which now contain a limitation that the biodegradable protein binds the hedgehog protein and releases said protein in a delayed manner. Applicants assert that the combination of references cited by the Examiner fail to render the claimed invention obvious, that Pepinsky et al. fail to disclose the particular combinations of elements that characterize the claimed invention, and that these deficiencies are not overcome by Easton or Usala, which provide nothing more than an invitation to one of skill in the art to attempt to arrive Applicant's invention. Applicants have amended the claims so that they are directed to a delayed release composition, and assert that such delayed release compositions were not contemplated by the prior art.

Applicants' arguments have been fully considered but are not deemed persuasive.

Pepinsky et al. teaches that the half-life of hedgehog is very short after systemic application and that multiple injections are required to achieve a robust response to the protein and that the possibility of formulation in liposomes provides a means of achieving a response with fewer treatments (column 38, line 62 to column 39, line 1), and that the proteins can be administered locally to the site of bone fractures to help heal those fractures (column 39, lines 20-22). Easton teaches that the compositions of the complex and methods of preparation can be varied and will result in complexes having different stabilities, pore sizes and uses (column 3, line 47 to column 4, line 28), and that examples of such applications include media to be used in the controlled release of physiologically active compounds (column 5, lines 50-55), and thus, teaches delayed release compositions. Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art to administer the hedgehog proteins of Pepinsky et al. in a carrier such as collagen that has been formulated to release the proteins slowly as taught by Easton, since Pepinsky teaches that systemically administered hedgehog proteins have short half-lives and that local application without the need for frequent application would be desirable under certain circumstances. There would be a reasonable expectation of success, since such controlled release formulations had been widely used in the field.

It is believed that all pertinent arguments have been answered.

***Conclusion***

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eileen B. O'Hara, whose telephone number is (703) 308-3312. The examiner can normally be reached on Monday through Friday from 10:00 AM to 6:30 PM. *Applicant is advised that effective January 23, 2004, the Examiner's phone number will be (571) 272-0878.*

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached at (703) 308-6564. *Applicant is advised that effective January 23, 2004, Yvonne Eyler's phone number will be (571) 272-0871.*

Official papers Before Final filed by RightFax should be directed to (703) 872-9306.

Official papers After Final filed by RightFax should be directed to (703) 872-9307.

Official papers filed by fax should be directed to (703) 308-4242.

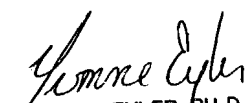
Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Eileen B. O'Hara, Ph.D.

Patent Examiner



BRUCE KISLIUK, DIRECTOR  
TECHNOLOGY CENTER 1600



YVONNE EYLER, PH.D.  
SUPERVISORY PATENT EXAMINER  
TECHNOLOGY CENTER 1600